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# Autogenic-Feedback Training: A Potential Treatment for Post-Flight Orthostatic Intolerance in Aerospace Crews

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## Summary

Postflight orthostatic intolerance has been identified as a serious biomedical problem associated with long duration exposure to microgravity in space. High priority has been given to the development of countermeasures for this disorder which are both effective and practical. A considerable body of clinical research has demonstrated that people can be taught to increase their own blood pressure voluntarily and that this is an effective treatment for chronic orthostatic intolerance in paralyzed patients. The present pilot study was designed to examine the feasibility of adding training in control of blood pressure to an existing preflight training program designed to facilitate astronaut adaptation to microgravity. Using an operant conditioning procedure, Autogenic-Feedback Training (AFT), three men and two women participated in four to nine (15-30 min) training sessions. At the end of training, the average increase in systolic and diastolic pressure, as well as mean arterial pressures that the subjects made, ranged between 20 and 50 mmHg under both supine and 45° head-up tilt conditions. These findings suggest that AFT may be a useful alternative treatment or supplement to existing approaches for preventing postflight orthostatic intolerance. Further, the use of operant conditioning methods for training cardiovascular responses may contribute to the general understanding of the mechanisms of orthostatic intolerance.

## Current Research on Postflight Orthostatic Intolerance

Postflight orthostatic intolerance is a biomedical problem which has significant impact on the health and safety of crewmembers exposed to sustained microgravity in space. Ground-based research designed to mimic the cardiovascular effects of spaceflight examine physiological responses to inactivity (or immobility) during protracted bed rest. Sandler (ref. 1) summarizes the findings of these investigations which describe characteristics of this syndrome which include (a) plasma volume loss of 15-20%; (b) total blood volume loss of 5-10%; (c) decrease in heart volume of 11% (after 20 days of bed rest); (d) decrease in left ventricular end diastolic volume of 6-11%; (e) reduced exercise tolerance; (f) reduced  $\text{VO}_2$  max; and (g) reduced orthostatic tolerance during standing, tilt, or lower body negative pressure (LBNP). Although comparatively little data are available on the biomedical condition of man in space, studies conducted on astronauts and cosmonauts during and after flight have shown physiological changes which are similar or identical to those observed in bed-rest studies (refs. 2-15).

Having evolved in the 1-gravity norm of Earth, the cardiovascular system can efficiently respond to shifts in body position. A gravity receptor system using information from muscle proprioceptors, vestibular organs, and mechanoreceptors (baroreceptors) operates continually to initiate changes in cardiovascular regulation as we interact with our environment. Under normal circumstances, there are three levels of defense to offset cardiovascular changes that occur with a shift of body position from supine to standing (ref. 1). Approximately 70% of the body's blood volume resides in the systemic veins. Upon standing, 700 ml of venous blood from the upper body shifts to deep intra- and intermuscular leg veins, with 200 ml going to the pelvis and gluteus maximus areas. The immediate response to this change in the distribution of blood is rapid contraction of the smooth muscle in the venous wall, movement of the diaphragm, and contraction of the lower limb muscles, combining to "squeeze" blood back up to the heart. Two other long-term events converge to maintain normal blood pressure and distribution. Plasma volume is increased or decreased as appropriate by the action of pre- and postcapillary sphincters, and by other mechanisms. And, when activated, neural or neurohumoral control stimulates sympathetic nerve activity or inhibits the release of potent hormonal regulators such as antidiuretic hormone.

When any one of these compensatory mechanisms is inadequate or retarded, orthostatic intolerance occurs with resultant fainting (vasovagal syncope) (ref. 1). The exact trigger for syncope is unknown, but the work of Epstein et al. (refs. 7, 16, and 17) strongly suggests a primary role for the cardiac ventricles. A significant shift of intravascular volume to the feet causes the ventricles to reach a critical minimal size. When this critical threshold for ventricular contraction is exceeded, nerve fibers in the wall discharge, thereby initiating the fainting process. Failure of the first or most immediate line of defense—vasomotor and skeletal muscle contractions of sufficient magnitude needed to prevent pooling of blood in the legs—plays a principal role in triggering the remaining defense mechanisms (ref. 1).

Considerable effort has been expended in searching for a means of preventing orthostatic intolerance. The greatest emphasis has been placed on testing the effects of strenuous isotonic and isometric exercises. Although some beneficial results of exercise are noted following bed rest, orthostatic intolerance was not significantly reduced (refs. 4, 5, and 18). The Russians have studied the use of electrical stimulation of muscle as a countermeasure, but its value is questionable (refs. 19 and 20). Several pharmacological agents have been tested as countermeasures, including central nervous system (CNS) stimulants

(e.g., amphetamine, strychnine, and caffeine), androgens (nerobol), and the calcium-blocking agent, isoptin (refs. 6, 10, and 21). These agents resulted in partial, yet inadequate, corrective effects on cardiovascular and electrolyte changes.

Short-term therapeutic effects have been seen where fluid loading (i.e., consuming 32 ounces of saline solution) prior to reentry of the Shuttle has enabled crewmembers to temporarily avoid syncope or pre-syncope symptoms postflight (ref. 2). Research is under way which examines the combined use of fluid loading with daily inflight exposure (4 hours per day) to lower body negative pressure (LBNP) (ref. 2). To date, the most effective method for managing the symptoms of (inactivity-induced) orthostatic intolerance is the use of a counter pressure garment (or g-suit) which mechanically prevents displacement of fluids to the lower extremities (ref. 22).

### **Training Voluntary Increases of Blood Pressure**

The importance of psychological processes in neurogenic orthostatic regulation has received relatively little attention. Our research group is investigating the potential of training people to voluntarily increase systolic and diastolic blood pressure as a treatment for orthostatic intolerance. The specific training method used in this study, Autogenic-Feedback Training (AFT), was developed as a potential treatment for space motion sickness in astronauts aboard the space shuttle (refs. 23-30). AFT is an operant conditioning paradigm which enables training control of multiple physiological responses simultaneously. The results of ground-based studies show that AFT is effective for controlling motion sickness in both men and women of different age groups and occupations, and that the training effects transfer across a variety of stimulus conditions (ref. 23).

Operant conditioning can be described simplistically as a trial-and-error learning process in which the response learned and performed must be followed by either a reward or a punishment (i.e., contingent reinforcement). When a novice is learning better voluntary control over where the basketball goes in shooting fouls, seeing the ball go through the hoop (success) serves as a reward, and seeing it miss (failure) serves as a punishment. If the novice were blindfolded so that he did not have any knowledge of the results of his shots, he would not learn. It was Miller's contention (ref. 31) that visceral and CNS events may be modified by contingent reinforcement in the same way overt behaviors or skeletal responses may be conditioned. Hence, the "same rules" apply for describing the process by which athletic skills are

acquired, as in the situation where an individual learns voluntary control of his own heart rate or the vasomotor activity of his hands. To learn control of a physiological response, the subject must be given a means of perceiving that response (e.g., external feedback in the form of a numerical display of heart rate).

The question as to the specific mechanism by which control of an autonomic response may be learned has spawned considerable basic research. When either classical or operant conditioning is used to modify a visceral response, there are a number of different ways that the effect can be produced (ref. 32). Skeletal responses may produce mechanical artifact in the measurement of the visceral response. For instance, contractions of the abdominal muscle may produce pressure changes in the intestine that can be mistaken for intestinal contractions (ref. 33). Skeletal muscles may produce purely mechanical effects on visceral processes. Yogis who claim the ability to stop their hearts actually perform valsalva maneuvers, building sufficient thoracic pressure to collapse the veins returning blood to the heart. Although heart sounds and pulse cannot be detected, the electrocardiogram shows that the heart still beats (ref. 34). Skeletal responses may stimulate a visceral reflex such as heart rate and blood pressure increased by isometric contractions (ref. 35). Any of these skeletally influenced responses may be learned but they do not indicate learning by the autonomic nervous system. In fact, they represent intervening variables in the investigation of visceral plasticity.

A series of clinical investigations was initiated on patients with generalized bodily paralysis who suffered from chronic orthostatic intolerance (refs. 32, 36, and 37). It was hypothesized that if learned control of blood pressure could be demonstrated in these individuals where skeletal influence was not a factor, then the basic research question of visceral plasticity could be examined and the therapeutic benefits of such training could be explored.

The first patient to receive training (ref. 36) had suffered complete transection of his spinal cord at T3, due to a gunshot wound. After 3 years of intensive physical therapy, this 31-year-old man was still unable to use leg braces preparatory for crutch walking because of pronounced orthostatic intolerance. During attempts at standing, his diastolic pressure would drop to below 30 mmHg, followed by syncope. Biofeedback training was administered during eleven one-hour sessions. Respiration, finger pulse volume, and ECG were monitored, but the only "feedback" device was a blood pressure system described by Tursky, Shapiro, and Schwartz (refs. 38-40). A cuff containing a microphone was placed over the brachial artery and inflated to just

above systolic pressure. When pressure increases occurred, Korotkoff sounds detected by the microphone tripped a Schmitt trigger, which caused a tone to sound. The subject's task was to keep the tone "on," hence raise his blood pressure. After training, he was able to produce increases in both systolic and diastolic pressures which averaged 48 mmHg. He has been walking with crutches ever since.

Another patient who had been confined to bed for 5 years because she fainted whenever elevated to a sitting position was also taught to voluntarily increase her blood pressure. Since her training was administered 12 years ago, she has been able to sit in a wheelchair throughout the day without recurrence of hypotensive episodes. Both of these patients were unusual in that they had failed to respond to extensive treatment by traditional physical therapy methods of gradual habituation to an increasingly vertical posture. For them, biofeedback was the only effective treatment.

The second study attempted a more detailed examination of the mechanism of learning blood pressure control (ref. 37). Twelve patients participated, four of whom had spinal lesions, four suffered from poliomyelitis and four with muscular dystrophy. After training, 11 out of 12 had achieved significant control of blood pressure, producing increases which ranged from 20 to 70 mmHg. In early sessions, voluntarily produced blood pressure increases were accompanied by increased heart rate; then, as diastolic pressure continued to rise, heart rate fell to (an average of) 16 beats per minute below the initial value, presumably as a result of the sinocardiac reflex. Finger pulse volume also showed vasoconstriction, suggesting that somehow these subjects had learned to reduce inhibitory impulses from the vagus nerve (since sympathetic innervation to vasomusculature was absent). But with additional training, control became more specific and pressure increases were produced with no significant change in pulse rate.

One of the few skeletal responses available to all of these patients is breathing, which can stimulate the receptive fields of cardiovascular reflexes in a number of ways, such as changing the  $\text{PCO}_2$  level of the blood. Voluntary increases in blood pressure, however, were not accompanied by either increases in respiration rate or volume, and  $\text{PCO}_2$  level remained virtually unchanged. When they were asked to make much larger changes in the rate of breathing, these changes had appropriate effects on  $\text{PCO}_2$  level and slight effects on heart rate, but virtually no effect on blood pressure. It seemed unlikely that voluntary increases in pressure were produced via hyper- or hypoventilation. When patients were asked to attempt to maximally contract both nonparalyzed and paralyzed

muscles, increases in heart rate and blood pressure occurred, although the pressure changes here were considerably smaller than those produced "on command," without any appreciable increases in muscle tension as measured by electromyography (EMG).

The results of these studies showed that patients could learn to produce increases in blood pressure ranging from 20 to 70 mmHg, with the consequence of eliminating their orthostatic intolerance. These studies succeeded in establishing that control of blood pressure can be learned independent of changes in skeletal musculature or respiration. They demonstrated also that training increases specificity of control, eventually eliminating accompanying pulse rate increases. And performance of these patients conformed to the cardinal "rule" of operant conditioning: skill increases with practice.

Other studies have been conducted by Shapiro and colleagues, in which normotensives subjects learned to modify their own systolic and diastolic blood pressure responses to postural challenge, (i.e., shift from sitting to standing position) (refs. 38–41). These studies utilized an improved blood pressure feedback system which enabled tracking systolic and diastolic pressure on each heart beat. In the first experiment, (ref. 39) the effects of training voluntary control of systolic blood pressure and heart rate during postural change was examined in three groups of men, ( $N = 10$  per group). In two groups, subjects were given feedback training to increase or decrease their systolic blood pressure. In the third group, subjects were simply asked to increase their blood pressure but were not given feedback about their performance. Voluntary control of systolic blood pressure was attempted while subjects were seated and during postural change from sitting to standing. Subjects were also instructed to maintain voluntary blood pressure control in subsequent no-feedback test trials. During postural change, voluntary control procedures caused significant alterations in tonic levels of systolic pressure, but phasic blood pressure reactivity was unaffected. With respect to the effect of postural changes on heart rate, both tonic and phasic treatment effects were observed. Blood pressure changes were observed in subjects given no feedback, but these were inconsistent and of significantly smaller magnitude than those observed when feedback was provided.

The second study (ref. 40) examined the effects of training voluntary control of diastolic blood pressure. Systolic blood pressure was also measured but was not displayed to subjects. Forty normotensives men were randomly assigned to four experimental conditions ( $N = 10$  per group), with the provision that mean systolic and diastolic blood pressure were approximately equivalent across conditions. Each subject participated in

a single 1.5 hour session. During the session, subjects were instructed to increase either diastolic blood pressure or heart rate, with or without appropriate feedback. The conditions were (1) diastolic blood pressure feedback, (2) diastolic blood pressure without feedback, (3) heart rate feedback; and (4) heart rate without feedback. With training, substantial increases in tonic levels were obtained for all three cardiovascular variables while sitting and during postural change. Changes produced were significantly higher when feedback was provided than in the no feedback conditions. When feedback was provided during postural shift, a distinct change in the phasic responses of blood pressure and heart rate was observed, in which pressure and heart rate increases occurred earlier (i.e., returning to recovery levels faster). Both of these studies succeeded in demonstrating that normotensive subjects could learn blood pressure control and the provision of feedback made this control more reliable; however, the magnitude of learned blood pressure increases were relatively small, averaging 10 mmHg.

### **Previous Applications of Training Control of Multiple Autonomic Responses**

For the past 19 years this laboratory has been dedicated to the development of a means for controlling space motion sickness symptoms. This disorder resembles motion sickness, and it affects 50% of all astronauts during the first few days of exposure to microgravity in space, and on return to Earth. Our primary objective has been to develop a method of training individuals to control their own physiological responses and thereby prevent the occurrence of motion sickness. Our method of treatment was AFT. AFT is actually a combined application of several physiological and perceptual training techniques, principal among these are autogenic therapy (ref. 42) and biofeedback (ref. 31). This combined-therapies approach produces a methodology which is appreciably more effective than either of these two techniques when used alone (refs. 24, 25, and 43). Autogenic exercises provide the subject with a specific set of instructions and method of concentration which are likely to produce the desired response. For example, self-suggestions of warmth in the hands and feet are associated with measurable increases in peripheral vasodilatation (ref. 43). Consequently, the time normally spent by the subject using a trial-and-error strategy is shortened and the initial probability of making a correct response is substantially increased. Biofeedback complements autogenic therapy by providing immediate sensory information to the subject about the magnitude and direction of a response. Operant conditioning procedures allow for more precise control of a response,

as the "reward" (or feedback) can be presented only as the subject makes gradually larger response changes in the desired direction. As a result, the ultimate effectiveness of training is significantly increased.

During a typical training session, subjects, are instructed to control a pattern of physiological responses and are given many different feedback displays (visual and auditory) simultaneously. Multiparameter feedback requires additional training in attending to a complex set of feedback signals. Verbal instructions by the experimenter are often required to direct the subject's attention to specific feedback signals and to advise him of alternative strategies when an inappropriate response has occurred. Included in these alternative strategies are elements of systematic desensitization and progressive relaxation of muscle tension monitored at several sites.

The rationale for using AFT to treat motion sickness was based on the observation that there are profound autonomic nervous system (ANS) changes associated with this disorder (refs. 26 and 27). Large individual differences in physiological response patterns to motion stimulation have been observed but these patterns are highly repeatable within individuals (ref. 27). Because motion sickness is characterized by disturbances in ANS function, involving many organ systems to varying degrees across individuals, it was necessary to develop a method for conditioning control of multiple responses simultaneously (refs. 24 and 25). Training was tailored for each subject, with emphasis placed on training control of those physiological variables that were most responsive to motion sickness stimulation. Hence, for different subjects, success in controlling motion sickness symptoms was achieved by training different physiological responses. Our original goal was to apply this training as a treatment for crewmembers aboard shuttle missions. It was therefore necessary to establish training procedures that were both effective and practical (refs. 23 and 28-30).

The results of this work have shown that AFT represents a superior method for training of physiological control because (a) it has been shown to be effective in a wide population of individuals; (b) it enables sufficient

magnitude of control necessary to significantly reduce the behavioral and physiological reactions to severe environmental stressors (e.g., motion sickness stimulation); (c) it produces learned effects which are persistent over time and are resistant to extinction (i.e., forgetting); and (d) it can be administered in as short a period of time as 6 hours. The U.S. Air Force used a similar form of AFT to treat pilots for whom all other methods had proved unsuccessful in combating persistent air sickness in high performance military planes (refs. 44 and 45). Those



studies showed that training transfers from the rotating chair on the ground to the variety of maneuvers in military flight well enough to return aircrew that otherwise would have been permanently grounded to active flying duty.

A NASA Life Sciences flight experiment to test AFT as a countermeasure for space motion sickness in Shuttle astronauts has been flown on two missions ( $N = 6$ ) (ref. 29). Preliminary results from spaceflight experiments have shown that subjects who have received AFT were better protected from severe symptom episodes in flight than control subjects who had taken anti-motion sickness medications. Final validation of the AFT treatment effect in space will require data on additional subjects ( $N = 16$ ).

## Hypotheses

The potential of this approach for developing a treatment for orthostatic intolerance in aerospace crews is apparent; however, a number of methodological issues must be addressed before it can be determined if this type of training can be applied in a practical and efficient manner for astronauts, who have considerable demands of their time prior to and during spaceflight missions. Because our research group was conducting preflight crew training for control of space motion sickness as part of a formal Life Sciences shuttle flight experiment, we had an opportunity to incorporate training for control of blood pressure into our existing schedule. As such, the present pilot study was designed to examine the feasibility of training aerospace crews to voluntarily increase their own blood pressure with and without an orthostatic stress. The specific hypotheses of this study were:

1. Subjects given AFT (multiple response conditioning) will significantly increase their blood pressure from baseline levels during both supine and  $45^\circ$  head-up tilt conditions.
2. Blood pressure increases with AFT will be of greater magnitude than produced previously by normotensives and will be achieved in significantly less time than was required to train paralyzed patients.

## Methods

### Subjects

Three men and two women between the ages of 32 and 42 participated in this study. All subjects were space shuttle crewmembers who were also participants in another experiment in which AFT was used as a treatment for motion and space motion sickness. Subjects were physi-

cally fit as determined by medical examination and their informed consent was obtained after the nature and possible consequences of the study had been fully explained to them. This study was approved by the human research review board at NASA Ames Research Center.

### Apparatus

Electrocardiogram (ECG) was monitored using disposable Ag/AgCl electrodes placed laterally beneath the left and right collar bones and on the left, fourth intercostal space. A computer-controlled blood pressure monitoring system was used to provide continuous feedback of both systolic and diastolic blood pressure on every heart beat (refs. 38–41). This non-invasive system used two blood pressure cuffs, mounted over the brachial arteries of the left and right arms; the validity of this device has been previously established in research which compared it to invasive measures of blood pressure in humans and animals (ref. 38).

First, blood pressure was measured with a manual cuff. Then the computer controlled cuff used for measuring systolic blood pressure was initially inflated to just above this systolic pressure level. Using the R wave of the ECG to initiate timing, cuff pressure automatically deflated or inflated, in 3 mmHg increments, as the system "searched" for the presence of Korotkoff sounds (K-sound) detected by a crystal microphone beneath the cuff. If the K-sound was present, cuff pressure was increased on the subsequent heart beat; if absent, cuff pressure was decreased. In this manner, it was possible to track blood pressure with each heart beat. The tracking cuff was inflated for a period of 1 minute at a time, alternating with deflation during 30-second "rest periods" to allow normal circulation to resume. The measurement of diastolic blood pressure (on the other arm) reversed this process; if a K-sound was detected, cuff pressure was reduced on the subsequent heart beat.

Additional physiological measures of respiration rate, heart rate, skin conductance, and blood flow to the hands were obtained using the autogenic-feedback system-2 (AFS-2). The AFS-2 is a portable belt-worn physiological monitoring system developed by NASA in support of spaceflight experiments. This system includes a garment, transducers, biomedical amplifiers, a digital wrist-worn feedback display, and a cassette tape recorder. The entire instrument is powered by a self-contained battery pack.

A tilt table was used as the orthostatic stimulus. Subjects were secured to the table with 10-inch wide canvas belts, placed across the chest beneath their arms and across the lower abdomen. A  $45^\circ$  head-up tilt was used to reduce the effects of leg muscle contractions on the blood pressure

responses. In this manner, subjects could be tilted without the need for maintaining their position with a foot board.

### Procedures

Subjects were tested individually at approximately the same time of day, in a dimly lit sound-isolated chamber which was temperature controlled ( $22.2^{\circ}\text{F} \pm 2^{\circ}\text{C}$ ). Each subject was given between four and nine (15–30 minute) daily blood pressure training sessions. Because other mission related training was conducted in parallel, participation in these sessions was contingent on each subject's available time. On the first day, all subjects remained supine for 30 minutes prior to testing while ECG electrodes were attached and blood pressure cuffs were positioned and calibrated. Baseline recordings were taken of resting supine heart rate and blood pressure. Following this 30-minute period, changes in these variables resulting from passive head-up tilt of  $45^{\circ}$  were recorded (two 3–5 minute trials with supine intertrial rest periods of comparable duration).

On subsequent days, after an initial 4-minute supine baseline, subjects were then provided with information of their own blood pressure in the form of a computer screen numerical display which updated on each heart beat and two mercury columns showing systolic and diastolic blood pressure, respectively. In addition, these subjects were provided feedback for their own respiration rates, heart rates, skin conductance, and blood flow to the hands using AFS-2. While supine, subjects were instructed to increase their own blood pressure and were given an opportunity to practice control. Because this was an exploratory study in which we tested the impact of training procedures on crew comfort as well as learning rates, training trials varied from 1 to 3 minutes in duration with comparable-duration intertrial rest periods. Further, subjects were instructed not to tense their muscles or modify breathing while attempting to control blood pressure. When blood pressure increases were demonstrated under supine conditions, subjects were again tilted to  $45^{\circ}$  head up and instructed to increase their blood pressure. Testing was terminated if subjects reported any discomfort from the inflated cuffs or the tilt conditions.

### Data Analyses

One-minute means of systolic and diastolic blood pressure were computed from the beat-to-beat measures, and mean arterial pressure (MAP) was calculated from these means. The equation used for calculating MAP was  $(\text{systolic} + 2(\text{diastolic}))/3$ . The mean scores were subjected to a repeated measures analysis of covariance (ANCOVA), with two within-subject factors

(conditions and time), and a covariate (1 minute of baseline preceding each condition) used to correct for individual differences in baseline levels. The conditions were  $45^{\circ}$  head-up tilt (Passive Tilt, no training), using AFT to increase blood pressure while supine (Supine BP Up), and using AFT to increase blood pressure during  $45^{\circ}$  head-up tilt (Tilt BP Up). The time factor was minutes 1 and 2 following the baseline minute for each condition.

Because the number of sessions varied across subjects, the number of trials in which these subjects were tested in each condition also varied. The 1-minute means were averaged across trials for each subject and a trials factor was not included in the analysis. Separate ANCOVAs were performed for systolic and diastolic blood pressure and for MAP. Reported significance levels were based on Greenhouse-Geisser adjustments for repeated measures. Planned comparisons on means (paired t-tests) were done to examine specific effects within and between conditions. An alpha level of 0.05 was used for all comparisons.

### Results

During supine and tilt conditions, the blood pressure tracking system was able to reliably measure blood pressure and heart rate on a beat-to-beat basis, and did not cause subjects any undue discomfort. Figure 1 shows the data of one subject during a training session. Data are presented as 1-minute means with systolic blood pressure read from the scale on the left side of the graph and diastolic blood pressure read from the scale on the right side of the graph. During this training session, following an initial 4-minute baseline (bsln) under supine conditions, the subject was instructed to increase and decrease his blood pressure in alternating 2-minute trials. Those trials marked "S" were conducted while the subject was supine and those marked "T" were conducted during  $45^{\circ}$  head-up tilt. The last 2-min trial of increasing blood pressure during tilt was followed by a supine 4-minute baseline.

During passive tilt, all subjects showed a gradual decline in systolic pressure and a corresponding increase in both diastolic pressure and heart rate. When subjects were instructed to raise their blood pressure from baseline levels, increases ranging between 20 and 50 mmHg were observed. Figure 2 shows the beat-to-beat blood pressure and heart rate data of a representative subject during passive tilt and while attempting to increase his blood pressure during tilt. The left side of each graph shows 1 minute of resting (supine) blood pressure and heart rate, followed by 1 minute of Passive Tilt. The right graph shows 1 minute of supine data followed by one minute of

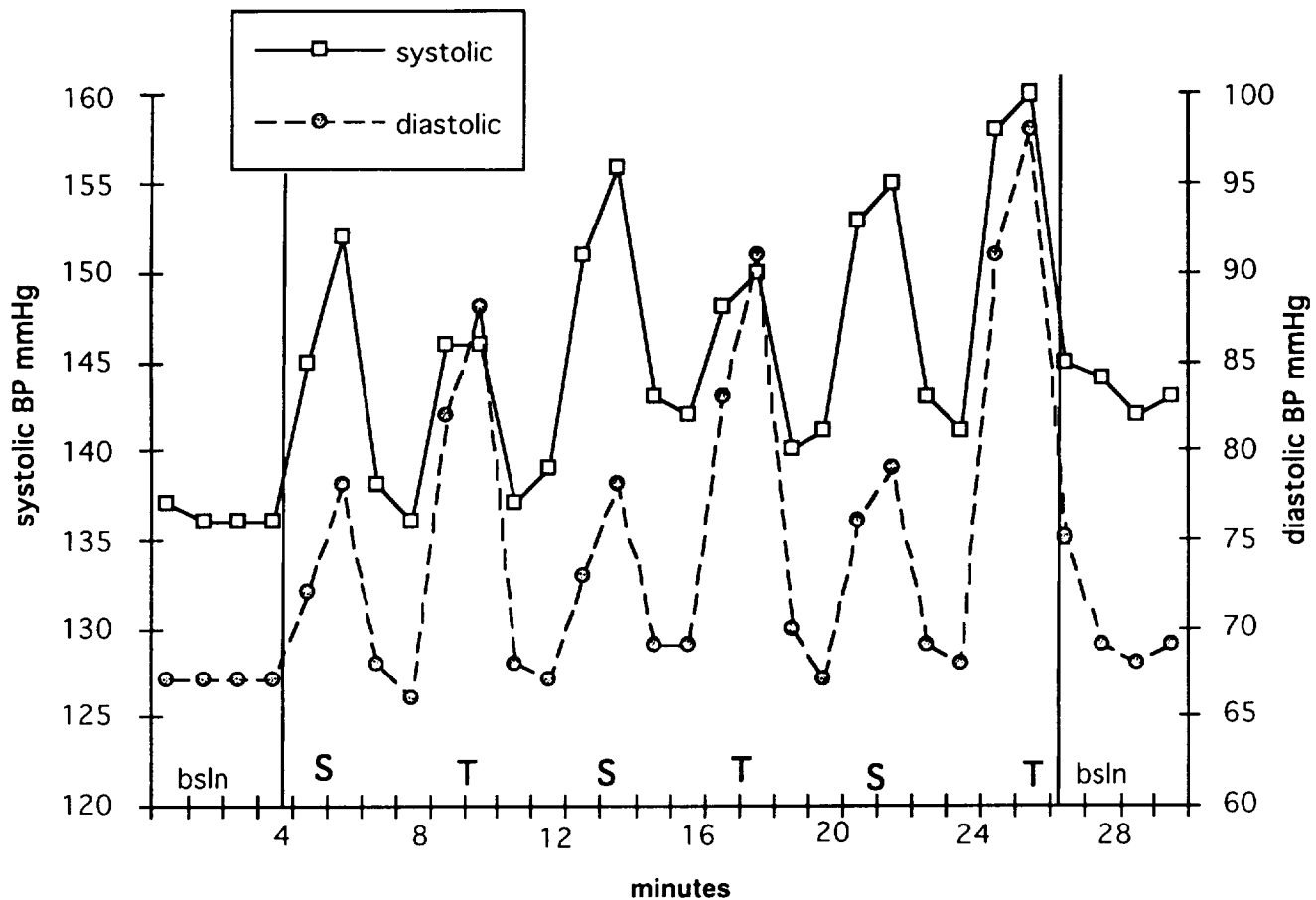


Figure 1. A 30-minute blood pressure training session subject 11, session #6.

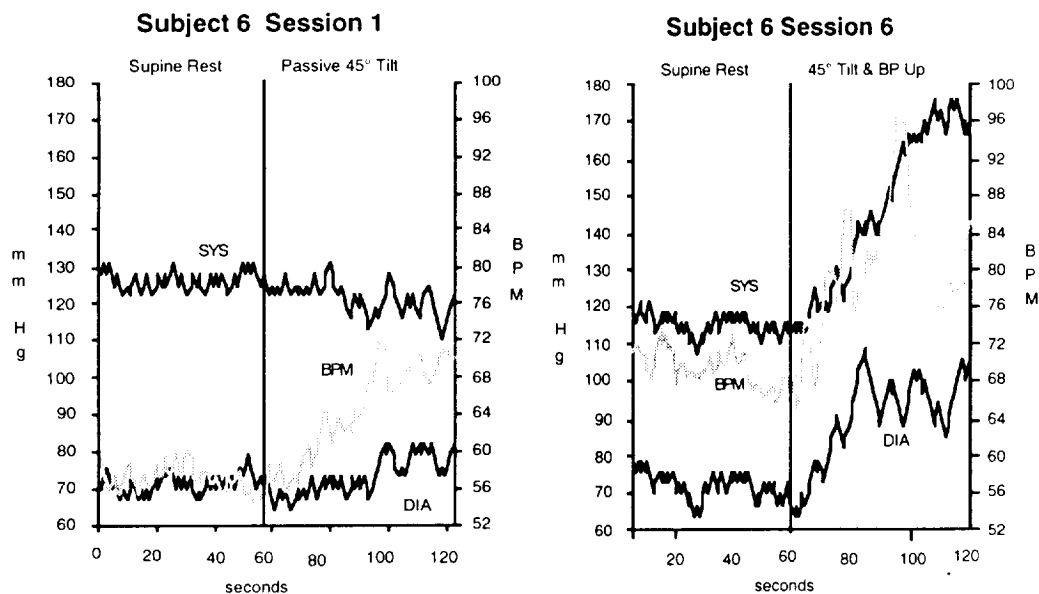


Figure 2. Tracking blood pressure beat-to-beat.

head-up tilt while the subject attempted to increase his blood pressure. The upper jagged line represents systolic blood pressure and the lower jagged line is diastolic blood pressure (read axis on left, mmHg). The thin line is heart rate (read axis on right, bpm = beats per minute). This subject was able to voluntarily increase his blood pressure during tilt by (maximally) 50 mmHg. Heart rate showed an initial increase from 68 to 96 beats per minute, followed by a decrease while blood pressure levels remained high.

Figure 3 shows the group means and standard errors for systolic and diastolic blood pressure during each

condition. Results from the ANCOVA for systolic blood pressure showed significance for the main effect of conditions ( $F(2, 7) = 19.46, p < 0.0072$ ), and for the interaction of conditions and time ( $F(2, 8) = 7.27; p < 0.029$ ). Results for diastolic blood pressure and MAP showed a significant difference for conditions ( $F(2, 7) = 6.55, p < 0.05$ ;  $F(2, 7) = 24.42; p < 0.005$ , respectively), but the interaction of time and conditions was not significant. All comparisons (paired t-tests) were based on 4 degrees of freedom. Within-condition comparisons showed that systolic blood pressure was significantly higher than baseline levels during the Supine BP Up training condition

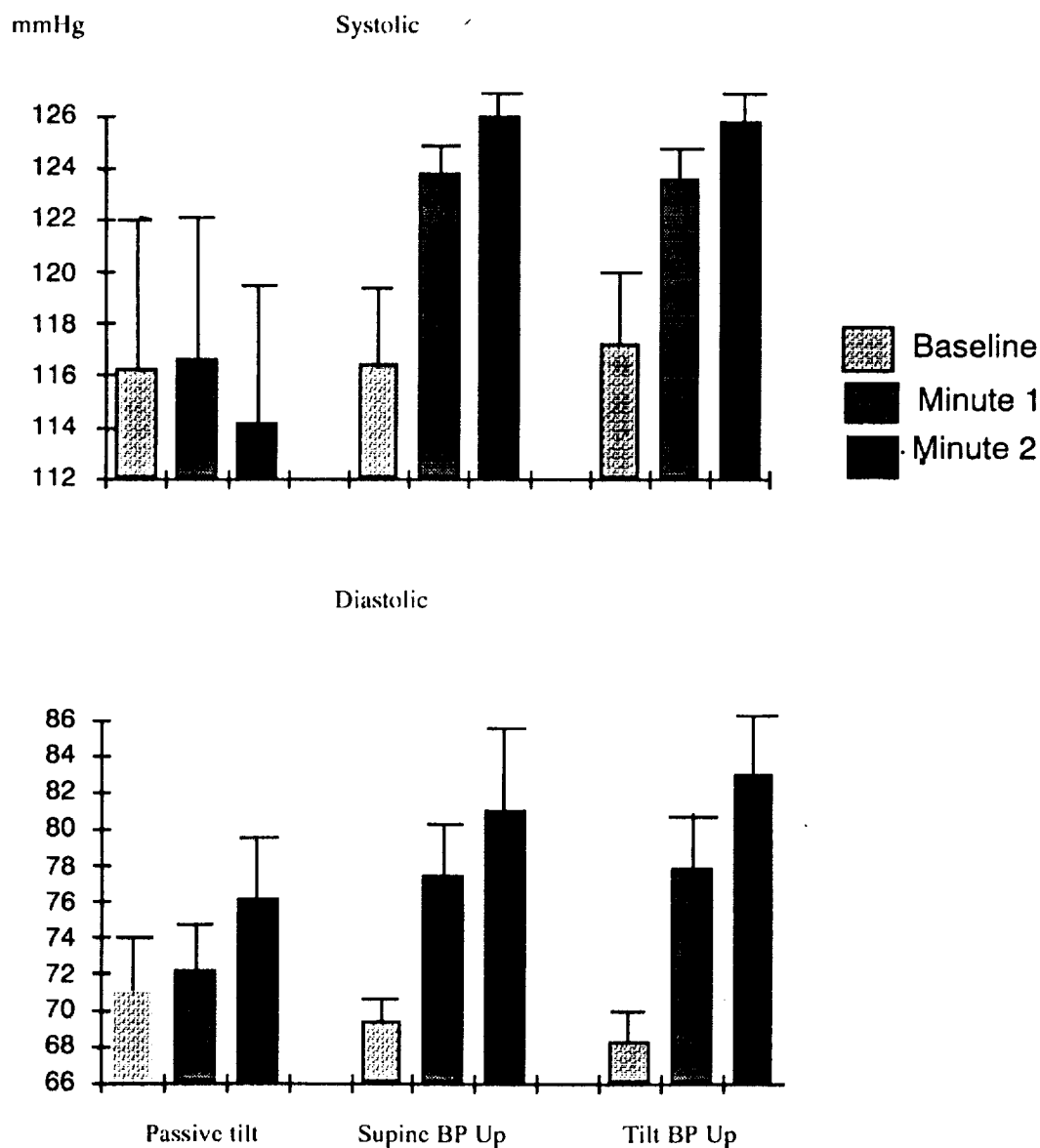


Figure 3. Group means ( $n = 5$ ) for systolic and diastolic blood pressure in all three experimental conditions.

(min 1,  $t = 3.09$ ,  $p < 0.01$ ; min 2,  $t = 4.11$ ,  $p < 0.01$ ), and the Tilt BP Up training condition (min 1,  $t = 3.14$ ,  $p < 0.03$ ; min 2,  $t = 3.71$ ,  $p < 0.02$ ). Diastolic blood pressure was also significantly higher than baseline during Supine BP Up (min 1,  $t = 3.95$ ,  $p < 0.02$ ; min 2,  $t = 4.56$ ,  $p < 0.01$ ) and Tilt BP Up (min 1,  $t = 4.76$ ,  $p < 0.009$ ; min 2,  $t = 4.69$ ,  $p < 0.009$ ). MAP showed a significant increase from baseline during Supine BP Up (min 1,  $t = 3.97$ ,  $p < 0.02$ ; min 2,  $t = 4.04$ ,  $p < 0.02$ ) and Tilt BP Up (min 1,  $t = 4.41$ ,  $p < 0.01$ ; min 2,  $t = 4.60$ ,  $p < 0.01$ ). There was no significant change from baseline during the Passive Tilt condition for systolic and diastolic blood pressure or MAP.

Between-condition comparisons showed that systolic and diastolic blood pressure (average of min 1 and 2) were significantly higher during Tilt BP Up than during Passive Tilt ( $t = 5.23$ ,  $p < 0.006$  and  $t = 5.74$ ,  $p < 0.005$ , respectively). Similarly, MAP was significantly higher during Tilt BP Up than during Passive Tilt ( $t = 6.02$ ,  $p < 0.004$ ). When the two training conditions Supine BP Up and Tilt BP Up were compared, there were no significant differences found for systolic, diastolic, or MAP.

## Discussion

This study successfully tested the feasibility of including training in the control of blood pressure into an existing preflight (AFT) training program for astronauts. This study demonstrates that learned control of clinically significant increases in blood pressure by normotensive individuals is possible in a relatively short period of time, and that the blood pressure tracking instrument used was effective for both detecting and training control of this response. Both hypotheses of this study have been confirmed: (1) subjects learned to significantly increase their blood pressure from baseline levels during both supine and tilt conditions, and (2) control of blood pressure was learned in less time than in paralyzed patients (refs. 2, 6, and 28) and resulted in larger magnitude changes than previously observed in normotensives (refs. 31 and 35).

Although encouraging, this study leaves many questions unanswered regarding the potential value of AFT as a countermeasure for postflight orthostatic intolerance. In the studies by Shapiro and colleagues (refs. 31 and 35) where the stimulus was a shift from sitting to standing position, the influence of skeletal musculature contractions on blood pressure changes was not investigated. Although skeletal muscle changes were not recorded in the present study, subjects were instructed not to contract their muscles. Further, it was

anticipated that the tilt-table stimulus used here as a postural challenge would produce much less muscle contraction than standing. Future studies on blood pressure training will control for the influence of skeletal musculature by monitoring electromyography at multiple sites.

In the studies on paralyzed patients, subjects were given between 20 and 30 hours of blood pressure training which produced increases ranging from 20 to 70 mmHg. Their control improved with practice, enabling them to maintain blood pressure over progressively longer periods of time and in the presence of distractions. In the present preliminary study, subjects produced maximal blood pressure increases between 20 and 50 mmHg with a maximum of only 3 hours of training. The training these subjects received was different from earlier studies, however, because blood pressure training sessions were conducted in parallel with AFT for another study (ref. 9). This involved an additional 6 hours of training for the control of heart rate, finger pulse volume, respiration rate, skin conductance, and muscle tension. The effect of training control of these variables on learning blood pressure control is unknown. Future studies will determine if feedback training for multiple physiological responses is more effective than blood pressure feedback alone, for the prevention of orthostatic intolerance.

None of the earlier studies on blood pressure control adequately investigated mechanisms by which the treatment effect was achieved. The cardiovascular responses to orthostatic stress are well known (ref. 1). Future studies will examine the effect of blood pressure training on total peripheral resistance, cardiac output, and contractility. These and other measures will help us understand underlying ANS mechanisms (i.e., changes in sympathetic or parasympathetic tone) in the treatment effect. In addition to studying ANS mechanisms in operant conditioning of blood pressure, we will examine the influence of plasma rennin activity (PRA) and vasopressin (AVP). In normotensives when shifting to an upright position, the resulting tendency for postural hypotension is buffered by a compensatory increase in sympathetic drive (which produces vasoconstriction and tachycardia), and activation of the rennin-angiotensin system (ref. 1). Before and after training, measurements of catecholamines, AVP and PRA (taken before and after orthostatic stress), should provide additional insight into the mechanisms by which operant conditioning of blood pressure increases might be achieved.

The passive 45° head-up tilt condition used in this study did not produce a significant change in blood

pressure or MAP, and therefore was not a good test for evaluating the effects of AFT as a potential treatment for orthostatic intolerance. It did provide, however, an initial assessment of the effects of AFT on blood pressure with and without orthostatic challenge. Future studies will utilize head up tilt of 60° and 90° for longer durations or exposure to lower body negative pressure (LBNP), thereby enabling more rigorous tests of the treatment effect, and identify its limits.

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13. ABSTRACT (Maximum 200 words)  Postflight orthostatic intolerance has been identified as a serious biomedical problem associated with long duration exposure to microgravity in space. High priority has been given to the development of countermeasures for this disorder which are both effective and practical. A considerable body of clinical research has demonstrated that people can be taught to increase their own blood pressure voluntarily and that this is an effective treatment for chronic orthostatic intolerance in paralyzed patients. The present pilot study was designed to examine the feasibility of adding training in control of blood pressure to an existing preflight training program designed to facilitate astronaut adaptation to microgravity. Using an operant conditioning procedure, Autogenic-Feedback Training (AFT), three men and two women participated in four to nine (15–30 training sessions. At the end of training, the average increase in systolic and diastolic pressure, as well as mean arterial pressures that the subjects made, ranged between 20 and 50 mmHg under both supine and 45° head-up tilt conditions. These finding suggest that AFT may be a useful alternative treatment or supplement to existing approaches for preventing postflight orthostatic intolerance. Further, the use of operant conditioning methods for training cardiovascular responses may contribute to the general understanding of the mechanisms of orthostatic intolerance.				
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